

INFORMATION DISCLOSURE STATEMENT

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In re Application of: Dominic P. BEHAN and Derek T. CHALMERS
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 For: *A Method of Identifying Modulators of Cell Surface Membrane Receptors Useful in the Treatment of Disease*
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Honorable Commissioner of Patents and Trademarks, Washington D.C. 20231 on July 8, 1998.

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 Patent Agent for the Applicants
 USPTO Reg. No. P-43,172

U.S. PATENT DOCUMENTS

Examiner's Initials	Cite No.	T ²
	NA	

Examiner Signature	Date Considered

OTHER DOCUMENTS – NON-PATENT LITERATURE DOCUMENTS

Examiner's Initials	Cite No.		T ²
3H		ALLA, S.A., et al (1996). Extracellular domains of the bradykinin B2 receptor involved in ligand binding and agonist sensing defined by anti-peptide antibodies. <i>J. Biol. Chem.</i> , 271, 1748-1755.	
↓		ADVENIER, C. et al (1992). Effects on the isolated human bronchus of SR 48968, a potent and selective nonpeptide antagonist of the neurokinin A (NK2) receptors. <i>Am. Rev. Respir. Dis.</i> , 146:5 Pt 1, 1177-81.	
✓		ALEXANDER, W.S., et al (1995). Point mutations within the dimer interface homology domain of c-Mpl induce constitutive receptor activity and tumorigenicity. <i>EMBO J.</i> , 14, 5569-78.	

Examiner Signature	Date Considered
<i>Zach Howard</i>	4/11/05

34		ARVANITIKIS, L., et al (1997). Human herpesvirus KSHV encodes a constitutively active G-protein-coupled receptor linked to cell proliferation. <i>Nature</i> , 385, 347-349.	
		BARKER, E.L., et al (1994). Constitutively active 5-hydroxytryptamine 2C receptors reveal novel inverse agonist activity of receptor ligands. <i>J. Biol. Chem.</i> , 269:16, 11687-11690.	
		BAXTER, G. (1995). 5-HT ₂ receptors: a family re-united? <i>Trends Pharmacol. Sci.</i> 16, 105-110.	
		BESMER, P., et al (1986). A new acute transforming feline retrovirus and relationship of its oncogene v-kit with the protein kinase gene family. <i>Nature</i> , 320, 415.	
		BLIN, N., et al (1995). Mapping of single amino acid residues required for selective activation of Gq/11 by the m3 muscarinic acetylcholine receptor. <i>J. Biol. Chem.</i> , 270, 17741-17748.	
		BOND, R. A., & BOUVIER, M., (1998). Inverse agonists and G-protein-coupled receptors. <i>Receptor-Based Drug Design</i> . Ed. Paul Leff. New York; M. Dekker. 363-377.	
		BOONE, C., et al (1993). Mutations that alter the third cytoplasmic loop of the a-factor receptor lead to a constitutive and hypersensitive phenotype. <i>Proc. Natl. Acad. Sci. (USA)</i> , 90:21, 9921-5.	
		BURSTEIN, E.S., et al (1996). Constitutive activation of chimeric m2/m5 muscarinic receptors and delineation of G-protein coupling selectivity domains. <i>Biochem Pharmacol</i> , 51:4, 539-44.	
		BURSTEIN, E.S., et al (1996). Amino acid side chains that define muscarinic receptor/G-protein coupling. Studies of the third intracellular loop. <i>J. Biol. Chem.</i> , 271:6, 2882-5.	
		BURSTEIN, E.S., et al (1995). Constitutive activation of muscarinic receptors by the G-protein Gq. <i>FEBS Lett.</i> , 363:3, 261-3.	
		BYLUND, D. (1994). International union of pharmacology nomenclature of adrenoceptors. <i>Pharmacol. Review.</i> , 46, 121-136.	
		CASEY, C., et al (1996). Constitutively active mutant 5-HT _{2A} serotonin receptors: inverse agonist activity of classical 5HT _{2A} antagonists. <i>Soc. Neurosci. Abstracts</i> # 699.10	
		CHEATHAM, B., et al (1993). Substitution of the erb-2 oncoprotein transmembrane domain activates the insulin receptor and modulates the action of insulin-receptor substrate. <i>Proc. Natl. Acad. Sci. (USA)</i> , 90, 7336-73340.	
		CHEN, T.S. et al (1993). Microbial hydroxylation and glucuronidation of the angiotensin II (AII) receptor antagonist MK 954. <i>J. Antibiot. (Tokyo)</i> , 46:1, 131-4.	
		CHEN, W., et al (1995). A colorimetric assay for measuring activation of G _s - and G _q - coupled signalling pathways. <i>Anal. Biochem.</i> , 226:2, 349-354.	
✓		CHIDIAC, P., et al (1994). Inverse agonist activity of beta-adrenergic antagonists. <i>J. Pharm. Expt. Ther.</i> , 45, 490-499.	

Examiner Signature	<i>Zach Howard</i>	Date Considered	4/11/05
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ZH	1	CLOZEL, M. et al (1993). In vivo pharmacology of Ro 46-2005, the first synthetic nonpeptide endothelin receptor antagonist: implications for endothelin physiology. J. Cardiovasc. Pharmacol., 22 Suppl 8:, S377-9.	1
J		COLLESI, C., et al (1996). A splicing variant of the RON transcript induces constitutive tyrosine kinase activity and an invasive phenotype. Mol. & Cellular Biol., 16, 5518-5526.	
		COOPER, C.S., et al (1984). Molecular cloning of a new transforming gene from a chemically transformed human cell line. Nature, 311, 29-33.	
		DESBLOS-MOULTON, C. et al (1996). Deletion of Asn281 in the -su b unit of the human insulin receptor causes constitutive activation of the receptor and insulin desensitization. J. Clin. Endocrinol. Metab., 81, 719-727.	
		DI RENZO, M.F., et al (1991). Expression of the Met/HGF receptor in normal and neoplastic human. Oncogene, 6:11, 1997-2003.	
		DI RENZO, M.F., et al (1992). Overexpression of the c-Met/HGF receptor gene in human thyroid carcinomas. Oncogene, 7, 2549-2553.	
		DUPREZ, L., et al (1994). Germline mutations in the thyrotropin receptor gene cause non-autoimmune autosomal dominant hyperthyroidism. Nature Genetics, 7, 396-401.	
		EGGERICKX, D., et al (1995). Molecular cloning of an orphan G-protein-coupled receptor that constitutively activates adenylate cyclase. Biochem. J., 389, 837-843.	
		EVANS, B.E. et al (1992). Orally active, nonpeptide oxytocin antagonists. J. Med. Chem., 35:21, 3919-27.	
		FU, M., et al (1994). Functional autoimmune epitope on alpha1-adrenergic receptors in patients with malignant hypertension. Lancet, 344, 1660-1663.	
		FURITSU, T., et al (1993). Identification of mutations in the coding sequence of the proto-oncogene c-kit in a human mast cell leukemia cell line causing ligand-independent activation of c-kit product. J. Clin. Invest., 92, 1736.	
		GELLAI, M. et al (1995). Nonpeptide endothelin receptor antagonists. V: Prevention and reversal of acute renal failure in the rat by SB 209670. J. Pharmacol. Exp. Ther., 275:1, 200-6.	
		GITTER, B.D. et al (1995). Pharmacological characterization of LY303870: a novel, potent and selective nonpeptide substance P (neurokinin-1) receptor antagonist. J. Pharmacol. Exp. Ther., 275:2, 737-44.	
		GOUILLEUX-GRUART, V., (1996). STAT-related transcription factors are constitutively activated in peripheral blood cells from acute leukemia patients. Blood, 87:5, 1692-7.	
		HANSSON, J.H., et al (1995). Hypertension caused by a truncated epithelial sodium channel gamma subunit: genetic heterogeneity of Liddle syndrome. Nat. Genet., 11:1, 76-82.	
✓		HASEGAWA, H., et al (1996). Two isoforms of the prostaglandin E receptor EP3 subtype different in agonist-independent constitutive activity. J. Biol. Chem., 271:4, 1857-1860.	1

Examiner Signature	Zach Howard	Date Considered	4/11/05
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34		HENDLER, A.M. & OZANNE, B.W. (1984). Human squamous cell lung cancers express increased epidermal growth factor receptors. J. Clin. Invest., 74, 647-651.	
		HERRICK-DAVIS, K., et al (1996). Constitutively active 5HT _{2C} serotonin receptor created by site directed mutagenesis. Soc. Neuroscience abstract #699.18.	
		HIEBLE, J. (1995). International union of pharmacology. X. Recommendation for nomenclature of 1-adrenoceptors. Pharmacol. Review., 47, 267-270.	✓
		HILL, S. (1990). Distribution properties and functional characteristics of three classes of histamine receptor. Pharmacol. Review. 7, 1-51.	
		HOGGER, P. et al (1995). Activating and inactivating mutations in the N- and C-terminal I3 loop junctions of muscarinic acetylcholine Hm1 receptors. J. Biol. Chem., 270, 7405-7410.	
		IKEDA, H., et al (1991). Expression and functional role of the proto-oncogen c-kit in acute myeloblastic leukemia cells. Blood, 78, 2962.	
		IMURA, R. et al (1992). Inhibition by HS-142-1, a novel nonpeptide atrial natriuretic peptide antagonist of microbial origin, of atrial natriuretic peptide-induced relaxation of isolated rabbit aorta through the blockade of guanylyl cyclase-linked receptors. Mol. Pharmacol., 42:6, 982-90.	
		JAKUB/EIK, J., et al (1995). Constitutive activity of the M1-M4 subtypes of muscarinic receptors in transfected CHO cells and of muscarinic receptors in the heart cells revealed by negative antagonists. FEBS Lett, 377:2, 275-9.	
		KJELSBERG, M.A., et al (1992). Constitutive activation of the alpha 1B-adrenergic receptor by all amino acid substitutions at a single site. J. Biol. Chem., 267, 1430-1433.	
		KNAPP, R. (1995). Molecular biology and pharmacology of cloned opioid receptors. FASEB J. 9, 516-525.	
		KOSUGI, S., et al (1995). Characterization of heterogenous mutations causing constitutive activation of the luteinizing hormone receptor in familial male precocious puberty. Human Molecular Genetics, 4:2, 183-188.	
		KOSUGI, S., et al (1993). Identification of thyroid-stimulating antibody-specific interaction sites in the N-terminal region of the thyrotropin receptor. Molecular Endocrinology, 7, 114-130.	
		KRAUS, M.H., et al (1993). Demonstration of ligand-independent signalling by the erbB-3 tyrosine kinase and its constitutive activation in human breast tumor cells. Proc. Natl. Acad. Sci. (USA), 90, 2900-4.	
		KUDLACZ, E.M. et al (1996). In vitro and in vivo characterization of MDL 105,212A, a nonpeptide NK-1/NK-2 tachykinin receptor antagonist. J. Pharmacol. Exp. Ther., 277:2, 840-51.	
✓		KURIU, A., et al (1991). Proliferation of human myeloid leukemia cell line associated with the tyrosine phosphorylation and activation of the proto-oncogene c-kit product. Blood, 78, 2834.	

Examiner Signature	<i>John Howard</i>	Date Considered	4/11/05
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341		LABBE-JULLIE, C. (1994). Effect of the nonpeptide neurotensin antagonist, SR 48692, and two enantiomeric analogs, SR 48527 and SR 49711, on neurotensin binding and contractile responses in guinea pig ileum and colon. <i>J. Pharmacol. Exp. Ther.</i> , 271:1, 267-76.	
		LATRONICO, A.C., et al (1995). A novel mutation of the luteinizing hormone receptor gene causing male gonadotropin-independent precocious puberty. <i>J. Clin. Endocrinol. Metab.</i> , 80, 2490-2494.	
		LAUE, L., et al (1995). Genetic heterogeneity of constitutively activating mutations of the human luteinizing hormone receptor in familial male-limited precocious puberty. <i>Proc. Natl. Acad. Sci. (USA)</i> , 92, 1906-1910.	
		LØVLIE, R., et al (1996). The Ca(2+)-sensing receptor gene (PCAR1) mutation T151M in isolated autosomal dominant hypoparathyroidism. <i>Hum. Genet.</i> , 98:2, 129-33.	
		LEFKOWITZ, R., et al (1993). Constitutive activity of receptors coupled to guanine nucleotide regulatory proteins. <i>Trends Pharmacol. Sci.</i> , 14, 300-307.	
		LIBERMANN, T.A., et al (1985). Amplification, enhanced expression and possible rearrangement of EGF receptor gene in primary human brain tumors of glial origin. <i>Nature</i> , 313, 144-147.	
		LIU, C., et al (1992). Overexpression of c-met proto-oncogene but not epidermal growth factor receptor or c-erbB-2 in primary human colorectal carcinomas. <i>Oncogene</i> , 7:1, 181-185.	
		LIU, J., et al (1996). Molecular mechanisms involved in muscarinic acetylcholine receptor-mediated G protein activation studied by insertion mutagenesis. <i>J. Biol. Chem.</i> , 271:11, 6172-6178.	
		LONARDO, F., et al (1990). The normal erb-2 product is an atypical receptor-like tyrosine kinase with constitutive activity in the absence of ligand. <i>The new Biologist</i> , 2:11, 992-1003.	
		MAENHAUT, C., et al (1990). RCD8 codes for an adenosine A2 receptor with physiological constitutive activity. <i>Biochem. Biophys. Res. Com.</i> , 173:3, 1169-1178.	
		MANN, J., et al (1986). Increased serotonin ₂ and beta-adrenergic receptor binding in the frontal cortices of suicide victims. <i>Arch. Gen. Psychiat.</i> 43, 954-959.	
		MARTONE, R.L. et al (1996). Human CRF receptor chimeras: mapping of ligand binding determinants. Abstract 609.8. 26 th meeting for the society of neuroscience, Washington, D.C., November 16-21, 1996.	
		MAGNUSSON, Y., et al (1994). Autoimmunity in idiopathic dilated cardiomyopathy. <i>Circulation</i> , 89, 2760-2767.	
✓		MATUS-LEBOVITCH, N., et al (1995). Truncation of the thyrotropin-releasing hormone receptor carboxy tail causes constitutive activity and leads to impaired responsiveness in <i>Xenopus</i> oocytes and AtT20 cells. <i>J. Biol. Chem.</i> , 270:3, 1041-1047.	

Examiner Signature	Zach Howard	Date Considered	4/11/05
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34		MYLES, G.M., et al (1994). Tyrosine 569 in the c-fms juxtamembrane domain is essential for kinase activity and macrophage colony-stimulating factor-dependent internalization. Mol. Cell. Biol., 14, 4843.	1
		NANEVICZ, T., et al (1996). Thrombin receptor activating mutations. J. Biol Chem., 271, 702-706.	
		NATALI, P.G., et al (1993). Expression of the c-Met/HGF receptor in human melanocytic neoplasms: demonstration of the relationship to malignant melanoma tumor progression. Br. J. Cancer, 68:4, 746-750.	
		NEILSON, K.M., et al (1995). Constitutive activation of fibroblast growth factor receptor-2 by a point mutation associated with Crouzon syndrome. J. Biol. Chem., 270:44, 26037-26040.	
		ODA, S. et al (1992). Pharmacological profile of HS-142-1, a novel nonpeptide atrial natriuretic peptide (ANP) antagonist of microbial origin. II. Restoration by HS-142-1 of ANP-induced inhibition of aldosterone production in adrenal glomerulosa cells. J. Pharmacol. Exp. Ther., 263:1, 241-5.	
		O'DOWD, B.F., et al (1988). Site-directed mutagenesis of the cytoplasmic domains of the human BETA ₂ -adrenergic receptor. J. Biol. Chem., 263, 15985-15992.	
		PALKOWITZ, A.D. et al (1994). Structural evolution and pharmacology of a novel series of triacid angiotensin II receptor antagonists. J. Med. Chem., 37:26, 4508-21.	
		PARENT, J., et al (1996). Mutations of two adjacent amino acids generate inactive and constitutively active forms of the human platelet-activating factor receptor. J. Biol. Chem., 271:14, 7949-7955.	
		PARFITT, A.M., et al (1996). Hypercalcemia due to constitutive activity of the parathyroid hormone (PTH)/PTH-related peptide receptor: comparison with primary hyperparathyroidism. J. Clin. Endocr. Metab., 81, 3584-3588.	
		PARMA, J., et al (1993). Somatic mutations in the thyrotropin receptor gene cause hyperfunctioning thyroid adenomas. Nature, 365, 649-651.	
		PEI, G., et al (1994). A constitutive active mutant BETA ₂ -adrenergic receptor is constitutively desensitized and phosphorylated. Proc. Natl. Acad. Sci. (USA), 91, 2699-2702.	
		PENDLEY, C.E. et al (1993). The gastrin/cholecystokinin-B receptor antagonist L-365,260 reduces basal acid secretion and prevents gastrointestinal damage induced by aspirin, ethanol and cysteamine in the rat. J Pharmacol Exp Ther, 265:3, 1348-54.	
		PEROUTKA, S. (1995). Serotonin receptor subtypes. Their evolution and clinical relevance. CNS Drugs. 4, 19-28.	
✓		PETTIBONE, D.J. & CLINESCHMIDT, B.V. (1993). Development and pharmacological assessment of novel peptide and nonpeptide oxytocin antagonists. Regul Pept, 29, 45:1-2.	1

Examiner Signature	Zach Howard	Date Considered	4/11/05
-----------------------	-------------	--------------------	---------

34		PRAT, M.P., et al (1991). The receptor encoded by the human C-MET oncogene is expressed in hepatocytes, epithelial cells and solid tumors. <i>Int. J. Cancer</i> , 49, 323-328.	
		PREZEAU, L., et al (1996). Changes in the carboxy-terminal domain of metabotropic glutamate receptor 1 by alternate splicing generate receptors with differing agonist-independent activity. <i>Mol. Pharmacol.</i> , 49, 422-429.	
		RAKOVSKA, A. et al (1993). Effect of loxiglumide (CR 1505) on CCK-induced contractions and 3H-acetylcholine release from guinea-pig gallbladder. <i>Neuropeptides</i> , 25:5, 271-6.	
		De Dios, I. & Manso, M.A. (1994). Effect of L-364,718 (CCK receptor antagonist) on exocrine pancreatic secretion of hydrocortisone-treated rats. <i>Pancreas</i> , 9:2, 212-8.	
		REN, Q., et al (1993). Constitutive active mutants of the ALPHA ₂ -adrenergic receptor. <i>J. Biol. Chem.</i> , 268, 16483-16487.	
		REYNOLDS, E.E. (1995). Pharmacological characterization of PD 156707, an orally active ETA receptor antagonist. <i>J. Pharmacol. Exp. Ther.</i> , 273:3, 1410-7.	
		ROBBINS, L.S., et al (1993). Pigmentation phenotypes of variant extension locus alleles result from point mutations that alter MSH receptor function. <i>Cell</i> , 72, 827-834.	
		RONG, S., et al (1993). Met expression and sarcoma tumorigenicity. <i>Cancer Res.</i> , 53:22, 5355-60.	
		SAMAMA, P., et al (1993a). A mutation-induced activation state of the B2-adrenergic receptor. <i>J. Biol. Chem.</i> , 268:7, 4625-36.	
		SAUTEL, M. et al (1996). Neuropeptide Y and the nonpeptide antagonist BIBP 3226 share an overlapping binding site at the human Y1 receptor. <i>Mol. Pharmacol.</i> , 50:2, 285-92.	
		SAWUTZ, D.G. et al (1995). Pharmacology and structure—activity relationships of the nonpeptide bradykinin receptor antagonist WIN 64338. <i>Can. J. Physiol. Pharmacol.</i> , 73:7, 805-11.	
		SCHEER, A. & COTECCHIA, S., (1997). Constitutively active G protein-coupled receptors: potential mechanisms of receptor activation. <i>J. Receptor & Signal Transduction Research</i> , 17(1-3), 57-73.	
		SCHEER, A., et al (1997). The activation process of the 1B-adrenergic receptor: potential role of protonation and hydrophobicity of a highly conserved aspartate. <i>Proc. Natl. Acad. Sci. (USA)</i> , 94, 808-813.	
		SCHWINN, D.A., et al (1995). Cloning and pharmacological characterization of human Alpha-1 adrenergic receptors: sequence corrections and direct comparison with other species homologues. <i>The J. Pharmacol.</i> , 272, 134-142.	
		SCHILD, L., et al (1995). A mutation in the epithelial sodium channel causing Liddle disease increases channel activity in the <i>Xenopus laevis</i> oocyte expression system. <i>Proc. Natl. Acad. Sci. (USA)</i> , 92, 5699-703.	
✓		SEEMAN, P. & VAN TOL, H. (1994). Dopamine receptor pharmacology. <i>Trends Pharmacol. Sci.</i> 15, 264-270.	

Examiner Signature	Zach Howard	Date Considered	4/11/05
-----------------------	-------------	--------------------	---------

34		SEEMAN, P. (1993). Dopamine D4 receptors elevated in schizophrenia. <i>Nature</i> , 365, 441-445.	
		SERRADEIL-LE GAL, C., et al (1993). Biochemical and pharmacological properties of SR 49059, a new, potent, nonpeptide antagonist of rat and human vasopressin V1a receptors. <i>J. Clin. Invest.</i> , 92:1, 224-31.	
		SHARIF, M., et al (1994). Malignant transformation by G protein-coupled hormone receptors. <i>Molecular & Cellular Endocrinology</i> , 100, 115-119.	
		SHOWERS, M.O., et al (1992). Activation of the erythropoietin receptor by the Friend spleen focus-forming virus gp55 glycoprotein induces constitutive protein tyrosine phosphorylation. <i>Blood</i> , 80, 3070-8.	
		SKINNER, R.H., et al (1994). Direct measurement of the binding of Ras to neurofibromin using scintillation proximity assay. <i>Anal. Biochem.</i> , 223, 259-265.	
		SLAMON, D.J., et al (1987). Human breast cancer: correlation of relapse and survival with amplification of the HER-2 neu oncogene. <i>Science</i> , 235, 177-182.	
		SLAMON, D.J., et al (1989). Studies of the HER-2/neu proto-oncogene in human breast and ovarian cancer. <i>Science</i> , 244, 707-712.	
		SOLOMON, Y., et al (1974). A highly sensitive adenylate cyclase assay. <i>Anal. Biochem.</i> , 58, 541-548.	
		SPIEGEL, A.M., et al (1995). Defects in G protein-coupled signal transduction in human disease. <i>Ann. Rev. Physiol.</i> , 58, 143-170.	
		TER LACK, A., et al (1995). Modelling and mutation studies on the histamine H1-receptor agonist binding site reveal different binding modes for H1-agonists: Asp116 (TM3) has a constitutive role in receptor stimulation. <i>J. Computer-aided molecular design</i> , 9, 319-330.	
		TIBERI, M. & CARON, M.G. (1994). High agonist-independent activity is a distinguishing feature of the dopamine D1B receptor subtype. <i>The J. Biol. Chem.</i> 269:45. 27925-27931.	
		TSUJIMURA, T., et al (1996). Constitutive activation of c-kit in FMA3 murine mastocytoma cells caused by a deletion of seven amino acids at the juxtamembrane domain. <i>Blood</i> , 87, 273-283.	
		WANG, Z., et al (1994). Constitutive opioid receptor activation as a regulatory mechanism underlying narcotic tolerance and dependence. <i>Life Sciences</i> , 54:22, 339-350.	
		WATOWICH, S.S., et al (1992). Homodimerization and constitutive activation of the erythropoietin receptor. <i>Proc. Natl. Acad. Sci. (USA)</i> , 89, 2140-4.	
		WEBER-NORDT, R.M., et al (1996). Constitutive activation of STAT proteins in primary lymphoid and myeloid leukemia cells and in Epstein-Barr virus (EBV)-related lymphoma cell lines. <i>Blood</i> , 88:3, 809-16.	
✓		WEBSTER, K. & DONOGHUE, J. (1996). Constitutive activation of fibroblast growth factor receptor 3 by the transmembrane point mutation found in achondroplasia. <i>The EMBO J.</i> , 15, 520-527.	

Examiner Signature	<i>John Howard</i>	Date Considered	<i>4/11/05</i>
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3H	1	XU, Y.H., et al (1984). Characterization of epidermal growth factor receptor gene expression in malignant and normal human cell lines. Proc. Natl. Acad. Sci. (USA), 81, 7308-7312.	1
↓	1	YAMADA, K., et al (1992). Substitution of the insulin receptor transmembrane domain with the c-neu/erb2 transmembrane domain constitutively activates the insulin receptor tyrosine kinase in vitro. J. Biol. Chem., 267, 12452-12461.	1
↓	1	ZHEN, Z., et al (1994). Structural and functional domains critical for constitutive activation of the HGF-receptor (<i>Met</i>). Oncogene, 9, 1691-1697.	1

Examiner Signature	Zach Howard	Date Considered	4/11/05
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